Notice of Allowability	Application No.	Applicant(s)	
	09/910,466	KONRADI ET AL.	
	Examiner	Art Unit	
	Tamthom N. Truong	1624	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address--

All claims being allowable, PROSECUTION ON THE MERITS IS (OR REMAINS) CLOSED in this application. If not included herewith (or previously mailed), a Notice of Allowance (PTOL-85) or other appropriate communication will be mailed in due course. **THIS NOTICE OF ALLOWABILITY IS NOT A GRANT OF PATENT RIGHTS.** This application is subject to withdrawal from issue at the initiative of the Office or upon petition by the applicant. See 37 CFR 1.313 and MPEP 1308.

1. ☒ This communication is responsive to *amendment of 01-08-04*.

2. ☒ The allowed claim(s) is/are *11,13-16 and 24-40*.

3. ☐ The drawings filed on _____ are accepted by the Examiner.

4. ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
   a) ☐ All b) ☐ Some* c) ☐ None of the:
      1. ☐ Certified copies of the priority documents have been received.
      2. ☐ Certified copies of the priority documents have been received in Application No. _____ .
      3. ☐ Copies of the certified copies of the priority documents have been received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

   * Certified copies not received: _____.

Applicant has THREE MONTHS FROM THE "MAILING DATE" of this communication to file a reply complying with the requirements noted below. Failure to timely comply will result in ABANDONMENT of this application.
THIS THREE-MONTH PERIOD IS NOT EXTENDABLE.

5. ☐ A SUBSTITUTE OATH OR DECLARATION must be submitted. Note the attached EXAMINER'S AMENDMENT or NOTICE OF INFORMAL PATENT APPLICATION (PTO-152) which gives reason(s) why the oath or declaration is deficient.

6. ☐ CORRECTED DRAWINGS (as "replacement sheets") must be submitted.
   (a) ☐ including changes required by the Notice of Draftsperson's Patent Drawing Review (PTO-948) attached
      1) ☐ hereto or 2) ☐ to Paper No./Mail Date _____.
   (b) ☐ including changes required by the attached Examiner's Amendment / Comment or in the Office action of Paper No./Mail Date _____.

   Identifying indicia such as the application number (see 37 CFR 1.84(c)) should be written on the drawings in the front (not the back) of each sheet. Replacement sheet(s) should be labeled as such in the header according to 37 CFR 1.121(d).

7. ☐ DEPOSIT OF and/or INFORMATION about the deposit of BIOLOGICAL MATERIAL must be submitted. Note the attached Examiner's comment regarding REQUIREMENT FOR THE DEPOSIT OF BIOLOGICAL MATERIAL.

Attachment(s)

1. ☒ Notice of References Cited (PTO-892)
2. ☐ Notice of Draftperson's Patent Drawing Review (PTO-948)
3. ☐ Information Disclosure Statements (PTO-1449 or PTO/SB/08), Paper No./Mail Date _____
4. ☐ Examiner's Comment Regarding Requirement for Deposit of Biological Material
5. ☐ Notice of Informal Patent Application (PTO-152)
6. ☒ Interview Summary (PTO-413), Paper No./Mail Date *attached* .
7. ☒ Examiner's Amendment/Comment
8. ☒ Examiner's Statement of Reasons for Allowance
9. ☐ Other _____.

EXAMINER'S AMENDMENT

An examiner's amendment to the record appears below. Should the changes and/or additions be unacceptable to applicant, an amendment may be filed as provided by 37 CFR 1.312. To ensure consideration of such an amendment, it MUST be submitted no later than the payment of the issue fee.

Authorization for this examiner's amendment was given in a telephone interview with Dr. Carol A. Stratford on 03-25-04.

The application has been amended as follows:

Cancel claims 17, and 19-23 without prejudice.

Claim 31: Page 11, lines 14-16, delete the entire definition of R21.

Allowable Subject Matter

Applicant's amendment of 01-08-04 has deleted the non-elected group. The cancellation of claims 1-10, 12, and 18 have overcome the previous rejections of 112/2nd paragraph, 102(b)/(e) and 103. Also, the amended claims 11, 13-16, and 24 have overcome the previous rejection of 112/2nd paragraph. With no other outstanding rejection, claims 11, 13-16, and 24-40 are allowed.

Reason for Allowance

The following is an examiner's statement of reasons for allowance:

The invention is drawn to compounds and pharmaceutical

compositions of formulae IIa, and IIc, which are substituted (pyrimidin-4-yl)alanine compounds. Note, the substituent "HetAr" is always substituted, which is not taught by the references of the previous 102 and 103 rejections. An update search yields the reference of **Spohr et. al.** (US 6,410,729 B1), which teaches substituted pyrimidinyl compounds. However, the disclosed compounds do not have a side chain equivalent to –NH-CH(CH_2-HetAr)-C(=O)-X. Thus, said reference does not anticipate or render obvious the instant invention.

Any comments considered necessary by applicant must be submitted no later than the payment of the issue fee and, to avoid processing delays, should preferably accompany the issue fee. Such submissions should be clearly labeled "Comments on Statement of Reasons for Allowance."

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Tamthom N. Truong whose telephone number is 571-272-0676. The examiner can normally be reached on M-T (~10 am ~ 8:30 pm) starting from February 22nd, 2004.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Mukund Shah can be reached at 571-272-0674. If you are unable to reach Dr. Shah within a 24 hour period, please contact James O. Wilson, Acting SPE of 1624, at 571-272-0661.

The fax phone numbers for the organization where this application or proceeding is assigned are 703-872-9306. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-1235.

T. Truong
March 25, 2004

RICHARD L. RAYMOND
PRIMARY EXAMINER
ART UNIT 1624

09/910,466 3/25/04

EXAMINER'S AMENDMENT

An examiner's amendment to the record appears below. Should the changes and/or additions be unacceptable to applicant, an amendment may be filed as provided by 37 CFR 1.312. To ensure consideration of such an amendment, it MUST be submitted no later than the payment of the issue fee.

Authorization for this examiner's amendment was given in a telephone interview with Dr. Carol A. Stratford on 03-25-04.

The application has been amended as follows:

Cancel claims 17, and 19-23 without prejudice.

Claim 31: Page 11, lines 14-16, delete the entire definition of R21.

(See attachment)

12. (canceled)

13. (currently amended) The compound of Claim 11 ~~or 12~~ wherein HetAr is a nitrogen containing heteroaryl group which is substituted with a group of formula -O-Z-$NR^{11}R^{11'}$ or -O-Z-R^{12} wherein R^{11} and $R^{11'}$ are independently selected from the group consisting of hydrogen, alkyl, substituted alkyl, cycloalkyl, substituted cycloalkyl, cycloalkenyl, substituted cycloalkenyl, heterocyclic, substituted heterocyclic, and where R^{11} and $R^{11'}$ are joined to form a heterocycle or a substituted heterocycle, R^{12} is selected from the group consisting of heterocycle and substituted heterocycle, and Z is selected from the group consisting of -C(O)- and -SO_2-.

14. (original) The compound of Claim 13 wherein the nitrogen containing heteroaryl group is substituted with a group of formula -$OC(O)NR^{11}R^{11'}$ wherein R^{11} and $R^{11'}$ are independently selected from the group consisting of alkyl or R^{11} and $R^{11'}$ are joined to form a heterocycle or a substituted heterocycle.

15. (original) The compound of Claim 14 wherein the nitrogen containing heteroaryl group is substituted with -$OC(O)N(CH_3)_2$ and is at the para position of the heteroaryl group.

16. (currently amended) The compound of Claim 11 ~~or 12~~ wherein HetAr is a nitrogen containing heteroaryl group which is substituted with an aryl or substituted aryl group.

Examiner's Amendment 3-25-04

17. (withdrawn) A method for treating a disease mediated by VLA-4 in a patient, which method comprises administering a pharmaceutical composition comprising a pharmaceutically acceptable carrier and a therapeutically effective amount of a compound of Claims 1-9, 11 or 12.

18. (canceled)

19. (withdrawn) A method for treating a disease mediated by VLA-4 in a patient, which method comprises administering a pharmaceutical composition comprising a pharmaceutically acceptable carrier and a therapeutically effective amount of a compound of Claim 10.

Examiner's Amendment 3-25-04

20. (withdrawn) A method for treating a disease mediated by VLA-4 in a patient, which method comprises administering a pharmaceutical composition comprising a pharmaceutically acceptable carrier and a therapeutically effective amount of a compound of Claim 13.

21. (withdrawn) A method for treating a disease mediated by VLA-4 in a patient, which method comprises administering a pharmaceutical composition comprising a pharmaceutically acceptable carrier and a therapeutically effective amount of a compound of 14.

22. (withdrawn) A method for treating a disease mediated by VLA-4 in a patient, which method comprises administering a pharmaceutical composition comprising a pharmaceutically acceptable carrier and a therapeutically effective amount of a compound of 15.

23. (withdrawn) A method for treating a disease mediated by VLA-4 in a patient, which method comprises administering a pharmaceutical composition comprising a pharmaceutically acceptable carrier and a therapeutically effective amount of a compound of Claim 16.

24. (currently amended) A pharmaceutical composition comprising a pharmaceutically acceptable carrier and a therapeutically effective amount of a compound of Claim [[10]] 11.

aminothiocarbonylamino, aminocarbonyloxy, oxycarbonylamino, oxythiocarbonylamino, thioamidino, thiocarbonylamino, aminosulfonylamino, aminosulfonyloxy, aminosulfonyl, oxysulfonylamino, aryl, substituted aryl, and oxysulfonyl;

R16 is selected from the group consisting of hydrogen, alkyl, substituted alkyl, alkoxy, substituted alkoxy, amino, substituted amino, cycloalkyl, substituted cycloalkyl, aryl, substituted aryl, heteroaryl, substituted heteroaryl, heterocyclic, substituted heterocyclic and halogen; and

R18 is selected from the group consisting of alkyl, substituted alkyl, alkoxy, substituted alkoxy, amino, substituted amino, cycloalkyl, substituted cycloalkyl, aryl, substituted aryl, heteroaryl, substituted heteroaryl, heterocyclic and substituted heterocyclic;

R20 is selected from the group consisting of hydrogen, alkyl, substituted alkyl, alkoxy, substituted alkoxy, cycloalkyl, substituted cycloalkyl, aryl, substituted aryl, heteroaryl, substituted heteroaryl, and heterocyclic, substituted heterocyclic and halogen;

Examiner's Amendment 3-25-04

[R21 is selected from the ~~group~~ consisting of alkyl, substituted alkyl, alkoxy, substituted alkoxy, ~~amino~~, substituted amino, cycloalkyl, substituted cycloalkyl, aryl, ~~substituted aryl~~, heterocyclic and substituted heterocyclic;]

X is hydroxyl; and

and enantiomers, diastereomers and pharmaceutically acceptable salts thereof.

32. (new) The compound of Claim 31 wherein HetAr is a nitrogen containing heteroaryl group which is substituted with a group of formula -O-Z-$NR^{11}R^{11'}$ or -O-Z-R^{12} wherein R^{11} and $R^{11'}$ are independently selected from the group consisting of hydrogen, alkyl, substituted alkyl, cycloalkyl, substituted cycloalkyl, cycloalkenyl, substituted cycloalkenyl, heterocyclic, substituted heterocyclic, and where R^{11} and $R^{11'}$ are joined to form a heterocycle or a substituted heterocycle, R^{12} is selected from the group consisting of heterocycle and substituted heterocycle, and Z is selected from the group consisting of -C(O)- and -SO_2-.

33. (new) The compound of Claim 32 wherein the nitrogen containing heteroaryl group is substituted with a group of formula -$OC(O)NR^{11}R^{11'}$ wherein R^{11} and $R^{11'}$ are